REMARKS

A. The claims are not anticipated by Simon *et al.*, WO 96/23080, Hembree *et al.*, or Shang *et al.*

Claims 8-11 stand rejected under 35 U.S.C. §102(b) as being anticipated by Simon *et al.* (1996, *Cancer Res.* 56:5369-74). Claims 8-12, 14, 16, and 18 stand rejected under 35 U.S.C. §102(b) as being anticipated by WO 96/23080. Claims 12-18 stand rejected under 35 U.S.C. §102(b) as being anticipated by either Hembree *et al.* (1996, *Cancer Res.* 56:1793-9) or Shang *et al.* (1999, *J. Biol. Chem.* 274:18005-10). Applicants respectfully traverse.

The Action asserts that Simon *et al.* (as evidenced by Montemurro *et al.*, 1999, *British J. of Haemotology* 107: 294-9) anticipates claims 8-11. Simon *et al.* teach that the retinoid PD 09059 *reduces* expression of urokinase-type plasminogen activator gene. This is in contrast with the teachings of the instant specification, that retinoids induce expression of urokinase-type plasminogen activator gene. The Action asserts that Montemurro *et al.* teaches that the identical promoter is induced by retinoids. However, the promoter taught by Montemurro is plasminogen activator inhibitor 2, while the promoter taught by Simon is the urokinase promoter. Therefore, the two references do not teach the same promoter. Furthermore, neither Simon *et al.* nor Montemurro *et al.* teaches that non-retinoid compounds can induce expression of genes that are induced by retinoids.

WO 96/23080 teaches that TIG1 can be used in screens to identify retinoids that stimulate TIG1 transcription (see page 32 of the application, for example). WO 96/23080 does not teach or suggest using the methods of the invention to identify non-retinoid compounds.

Without acquiescing to the correctness of these several bases of rejecting the pending claims, Applicants have amended independent claims 8 and 12 to recite that the compounds identified by the methods of the invention are *non-retinoid* compounds. None of the cited references teach non-retinoid compounds and thus cannot anticipate the invention claims.

Hembree *et al.* teach the effects of RXR-specific retinoids and RAR-specific retinoids on IGFBP-3 expression and activity in human ectocervical epithelial (ECE) cells. Shang *et al.* teach that expression of IGFBP-3 and retinoic acid receptor-β in MCF-7 cells can be induced in response to all-*trans*-retinoic acid and synthetic retinoids. Neither Hembree nor Shang teaches methods of screening for compounds. Both references merely demonstrate that retinoids can induce expression

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of IGFBP-3 in various cell types. These references cannot anticipate the instant claims either before or after the submitted amendments because the references do not teach screening methods or that non-retinoid compounds can induce expression of IGFBP-3.

Since none of the references cited in the Office Action anticipate the instant claims as amended, Applicants respectfully request that the rejections be withdrawn.

B. The claims are patentable under 35 U.S.C. §103.

Claims 8-16, and 18 stand rejected under 35 U.S.C. §103 as being unpatentable over the combination of four references: Adamo *et al.*, Miller, Han *et al.*, and US Pat. 5,795,726.

Applicants understand the reasoning behind the Patent Office determination of obviousness as follows. Adamo *et al.* teach that IGFBP-3 is expressed in MCF-7 breast cancer cells. Han *et al.* teach that *retinoids* can induce IGFBP-3 expression. Miller teaches that retinoids and retinoid analogs might be useful in treating cancer. The '726 patent generally teaches screening methods for identifying compounds (unrelated to the subject matter of the instant invention) that modulate human hepatic nuclear factor-1 (HNF-1) activity.

Applicants respectfully contend that the combination of these references does not render obvious claims 8-16 or 18 as filed. However, in an effort to expedite prosecution of the pending claims, Applicants amend herein independent claims 8 and 12 to recite that the compounds identified by the methods of the invention are *non-retinoid* compounds. Applicants note that none of these references teaches or suggests that *non-retinoid compounds* could be used to induce IGFBP-3 expression. Consequently, Applicants submit that these references when taken separately or in combination do not render the instant invention obvious, and respectfully request this rejection be withdrawn.

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CONCLUSIONS

Applicants respectfully contend that all conditions of patentability are met in the pending claims as amended. Allowance of the claims is thereby respectfully solicited.

The Examiner is invited to contact the undersigned representative by telephone at (312) 913-0001 if it is believed to be helpful.

Respectfully submitted,
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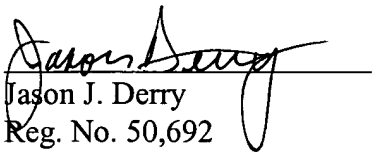
Date: June 26, 2003

By: 
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